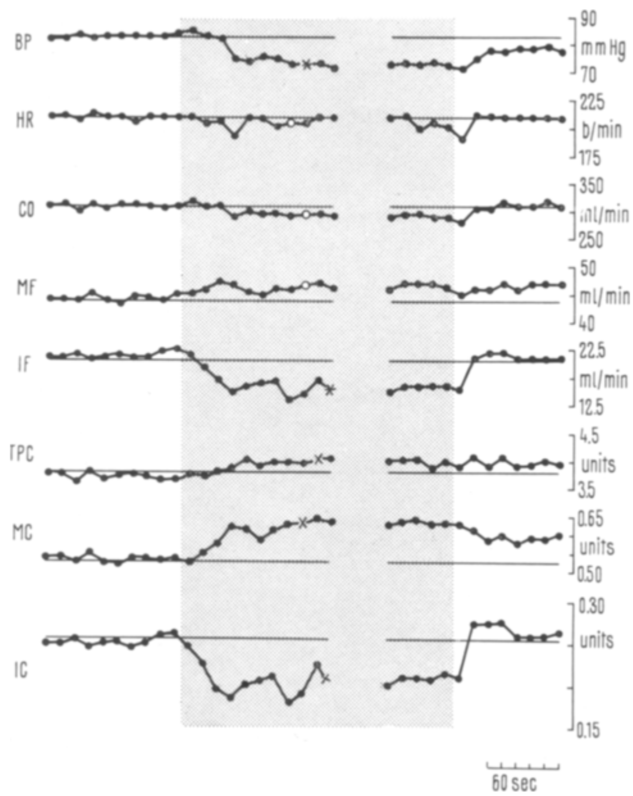
Regional Blood Flows During Desynchronized Sleep in the Cat[1]

Previous work of our group has shown that the fall in arterial pressure occurring in the cat during desynchronized sleep[2] (DS: a stage of sleep characterized by desynchronization of the electroencephalogram, disappearance of muscle tone and bursts of rapid eye movements and body twitches) largely depends on a dilatation of resistance vessels[3]. This vasodilatation is exaggerated by sinoaortic deafferentation[2,3], because of abolition of a buffering action exerted by carotid and aortic chemoceptors[4,5]. On the other hand, the vasodilatation is largely prevented by total sympathectomy[6], an observation indicating that it results from a decrease in sympathetic vasoconstrictor activity. It has not been known, however, whether the vasodilatation occurs in all vascular beds, and in all beds equally.

The present research has been directed to the study during DS of regional flow and conductance changes in the vascular beds of the superior mesenteric artery and external iliac artery, the first as an example of a visceral bed, and the second, after tying of its visceral branches, as an example of a mixed muscle-cutaneous bed. These peripheral flows were measured by means of electromagnetic probes (Statham, type Q 1.5 and 2 mm), which were implanted under Nembutal anaesthesia. At the same time a third probe (Statham, type K 6 or 7 mm) was implanted around the ascending aorta for the measurement of cardiac output less coronary flow. Probes chosen to fit the artery had already been calibrated with known blood flows, and were re-calibrated again after conclusion of experiments. The value of zero flow in the peripheral vessels was obtained by closing the descending aorta at a point above the root of the coeliac artery. These values were the same as others obtained by closing the vessels at a point distal to the probe. The instantaneous flows were continuously integrated by operational amplifiers automatically reset at 2-sec intervals. The heart rate was measured by a cardiotachometer and the arterial pressure by a Statham transducer connected to the right femoral artery by means of a rigid polyethylene tube. The cardiovascular variables were recorded on a 12-channel Grass P-7 polygraph along with right and left electroencephalograms, record of eye movements, and electromyograms of the neck and of the left hind limb. The recording session was held after the cat had completely recovered from the first surgery (usually at least 1 week). The registration was carried out while the cat was in a small electrically isolated sound-attenuating cage, and lasted for the amount of time required to obtain at least 6 episodes of DS. Each episode was analysed 2 min before and 2 min after the initiation of DS and 1 min before and 1 min after the arousal from the same, taking the value for 4 consecutive seconds out of every 12. The conductances were calculated in arbitrary units as a ratio of flow (in ml/min) divided by mean arterial pressure (in mmHg) during the same interval. The means of 6 episodes were graphed, and significance was tested by means of a t-test of differences comparing the values for a randomly chosen interval during the second minute of DS with those of a randomly chosen interval during the preceding synchronized sleep. All data reported here are from cats with intact sinoaortic reflexes.

The cardiovascular picture was similar in all of the 5 cats studied. As exemplified in the results from cat B in the Figure, we have confirmed the data we had previously reported[3]. In animals with intact sino-aortic reflexes, during DS there is a modest reduction in arterial pressure which is determined in part by a decrease in cardiac output due predominantly to a decrease in heart rate, and from an increase slightly more marked of total peripheral conductance.

The present results show that the peripheral vasodilatation does not take place in all beds. The superior mesenteric flow is increased during DS. This increase in flow, considering the simultaneous reduction in arterial pressure, is the result of a stronger and statistically significant increase of the conductance of the vascular bed. As compared with the mesenteric vasodilatation, the external iliac bed, however, undergoes an opposite change; its flow reduces markedly with a slope much steeper than that of the simultaneous reduction in arterial pressure, which



Means of measurements taken during 6 episodes of DS in cat B. Each dot represents the value for 4 consecutive sec out of every 12. Shaded area is DS (only first 2 min and last min analysed). Statistical significance indicated by asterisks ($p < 0.01$), crosses ($p < 0.05$), open circles ($p > 0.05$). BP, mean arterial pressure; HR, heart rate; CO, cardiac output; MF, superior mesenteric flow; IF, external iliac flow; TPC, total peripheral conductance; MC, superior mesenteric conductance; IC, external iliac conductance; b/min, beats per min.

1 This research has been sponsored by Consiglio Nazionale delle Ricerche (Gruppo di Medicina Sperimentale), and by a PHS fellowship to D. B. Adams.

2 M. GUAZZI and A. ZANCHETTI, Archs ital. Biol. *103*, 789 (1965).

3 T. KUMAZAWA, G. BACCELLI, M. GUAZZI, G. MANCIA and A. ZANCHETTI, Experientia *23*, 1021 (1967).

4 M. GUAZZI, G. BACCELLI and A. ZANCHETTI, Science *153*, 206 (1966).

5 M. GUAZZI, G. BACCELLI and A. ZANCHETTI, Am. J. Physiol. *214*, 969 (1968).

6 G. BACCELLI, M. GUAZZI, G. MANCIA and A. ZANCHETTI, in preparation.

represents a statistically significant reduction of conductance, i.e. a local vasoconstriction.

All of the cardiovascular variations measured tend in general to increase progressively during DS and to reach a type of plateau within the first 2 min and return to baseline values during arousal. In addition to these progressive and relatively continuous changes, however, there were also brief strong changes associated with the occurrence of rapid eye movements and diffuse intense muscle twitches. Modifications of arterial pressure and heart rate probably related to rapid eye movements and twitches have already been described by GASSEL et al.[7] and defined as phasic visceral changes of DS. We observed, in addition, a marked and immediate reduction of iliac conductance associated with each burst of rapid eye movements and with muscle twitches. These short-lasting iliac vasoconstrictions are superimposed upon the more continuous vasoconstriction of the iliac bed during DS.

The tonic and phasic decreases in external iliac flow and conductance are not due to constriction of visceral vessels, since the visceral branches of the external iliac artery were always tied off at their origin when the probes were implanted. The decrease also probably does not represent simply a vasoconstriction of cutaneous vessels, since an air pressure higher than systolic arterial pressure pumped into a plethysmograph cuff around the paw of the cat leaves unchanged both the continuous vasoconstriction during desynchronized sleep and also the phasic changes associated with rapid eye movements and twitches. It was assumed that the cuff pressure on the paw would eliminate most of the changes due to skin flow, since it is well known that the paw receives the major part of the neurally regulated cutaneous flow of the hind limb[8]. It is concluded that these diminutions of flow and conductance seen in the external iliac bed represent at least predominantly a vasoconstriction in the muscle components of the external iliac bed. According to recent preliminary data by REIS et al.[9], these changes in muscle circulation probably represent changes in red rather than white muscles.

In conclusion our results show that the increase in total peripheral conductance during desynchronized sleep in the cat is not due to a general vasodilatation in all peripheral beds. If other visceral beds change similarly to the superior mesenteric arterial bed, then the visceral beds are largely responsible for the phenomenon since superior mesenteric conductance increases at a greater rate than the total peripheral conductance. On the other hand, changes in muscle conductance are not responsible since they go in the opposite direction and reduce rather than augment the general effect. If we generalize from our previous experiments[6], it does not seem unlikely that mesenteric and visceral vasodilatation results from decreased sympathetic activity. The tonic and phasic constrictions of the muscle vessels are more difficult to explain, but, besides neural influences, mechanical and metabolic factors related to hypotonia and twitches should be considered.

Riassunto. Durante il sonno desincronizzato del gatto, non si ha una vasodilatazione generalizzata a tutti i letti vascolari. Mentre il distretto mesenterico si dilata, quello muscolare si costringe. La vasodilatazione viscerale dipende da una diminuita attività simpatica; per la vasocostrizione muscolare, invece, bisogna pensare, oltre che a meccanismi nervosi, anche a fattori meccanici e metabolici.

G. MANCIA, D. B. ADAMS,
G. BACCELLI and A. ZANCHETTI

Istituto di Ricerche Cardiovascolari dell'Università, 20122 Milano (Italy), 16 August 1968.

[7] M. M. GASSEL, B. GHELARDUCCI, P. L. MARCHIAFAVA and O. POMPEIANO, Archs ital. Biol. *102*, 530 (1964).
[8] G. STRÖM, Acta physiol. scand. *20*, Suppl. 70, 47 and 83 (1950).
[9] D. J. REIS, D. MOORHEAD and G. F. WOOTEN, Fedn Proc. Fedn Am. Socs exp. Biol. *27*, 224 (1968).

Nekrobiotische Zellveränderungen in der Hypophyse des Bachneunauges (*Lampetra planeri* Bloch) als Folge von Pilzinfektionen

Bei experimentell-morphologischen Untersuchungen an der Hypophyse des Bachneunauges (*Lampetra planeri* Bloch) fanden wir in der Mesoadenohypophyse ausschliesslich solcher Individuen, die infolge Hautverletzungen mit Schimmelpilzen (vermutlich Saprolegniaceen) befallen waren, eigenartige, mit Azokarmin kräftig anfärbbare Ablagerungen in mitunter recht beträchtlicher Zahl (Figur a). Eine erste histochemische Charakterisierung dieser Gebilde zeigte, dass sie reich an DNS sind. Im Regelfall sind ein oder mehrere tropfig-schollige, kräftig feulgenpositive, homogen erscheinende Körper unterschiedlicher Grösse von weniger voluminösen, feulgennegativen Substanzen umgeben, die sich mit Anilinblau tingieren lassen.

Wir nehmen an, dass die beschriebenen Strukturen das Resultat nekrobiotischer Kernveränderungen darstellen, die dem Formenkreis der Karyorrhexis zuzuordnen sind. In seiner Morphologie scheint sich der Prozess allerdings von den meist bei Säugetieren beschriebenen karyorrhektischen Kernalterationen[1] zu unterscheiden. Da sich nur selten Initialphasen des Nekrosevorganges (Figur b) – eine beginnende «Entmischung» des Kerninhaltes – auffinden lassen, muss angenommen werden, dass sich dieser sehr rasch vollzieht. Auch scheint das Cytoplasma von Beginn an in den Zelluntergang einbezogen zu werden. Die erwähnten feulgennegativen Substanzen sind als koagulierte Cytoplasmareste aufzufassen; ein die Aggregationen häufig umgebender optisch leer erscheinender Hof (Figur b) dürfte das Territorium des ehemaligen Zellkörpers markieren.

Der Zunächst nur vermutete ursächliche Zusammenhang zwischen Pilzinfektion und hypophysärer Zellnekrose konnte durch Induktion des Nekroseprozesses bei völlig gesunden Tieren mittels eines i.p. injizierten Pilzhyphenbreies experimentell bestätigt werden.

Von besonderem Interesse ist die Tatsache, dass sich die durch die Infektion hervorgerufenen pathologischen Veränderungen ausschliesslich auf die Mesoadenohypo-

[1] H.-W. ALTMANN und P. BANNASCH, Z. Zellforsch. *71*, 53 (1966).